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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/068,692	02/06/2002	Christopher J. O'Donnell	PC11080A	9227

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EXAMINER

COLEMAN, BRENDA LIBBY

ART UNIT PAPER NUMBER

1624

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/068,692

Applicant(s)

O'DONNELL ET AL.

Examiner

Brenda Coleman

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-20 are pending in the application.

This action is in response to applicants' amendment filed April 26, 2004. Claims 1, 6, 7 and 12-18 have been amended.

Response to Amendment

Applicant's amendments filed April 26, 2004 have been fully considered with the following effect:

1. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 1-4 and 6-15, the applicants' amendments and remarks have been fully considered but they are not found persuasive. In the present application Claims 1-4, 6 and 7 are deemed not enabled insofar as the generic formula of Claim 1 is exemplified only for the case where m is 2; o is 1 and n is 1. Thus, the embodiments of the generic formula where m is 1; o is 2 and n is 2 are not exemplified. The applicants' state "to begin with, it is noted that half of the meanings of the radicals within the scope of these three radicals are exemplified". The applicants' further stated, "Exemplification of half the meanings of the radicals is sufficient to enable those skilled in the art to make and use all members having the claimed meanings of m, o and n". However, half of the meanings of the radical m, o and n are not exemplified. There are more than two different structures form by the variables m, n and o. The applicants have only mentioned where m is 2; o is 1 and n is 1, which is exemplified in the claims and by examples and where m is 1; o is 2 and n is 2 which is not exemplified by examples. However, there are also the compounds where m is 1; o is 1 and n is 1; m is 2; o is 2 and n is 1; m is 1; o is 2 and n

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is 1; m is 2; o is 2 and n is 2; m is 1; o is 1 and n is 2; m is 2; o is 1 and n is 2; etc. in addition to the variables X, Y and Q which also limited in their exemplification.

With regards to the rejection of claims 9, 11, 13 and 15, the applicants' state that "many of the references recited in the specification establishing that α -7 nicotinic receptor agonists are therapeutic in the treatment of schizophrenia and other central nervous system disorders". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims where the disorder is treatable with a nicotinic acetylcholine receptor ligand. It is difficult to treat many of the disorders claimed herein. Recent studies on experimental and clinical pharmacology of nicotinic acetylcholine receptors cited in Annual Reports in Medicinal Chemistry indicate that the following disorders may be associated with nicotinic acetylcholine receptors: senile dementia of the Alzheimer's type, Parkinson's disease, Huntington's chorea, tardive dyskinesia, hyperkinesia, mania, depression, attention deficit disorder, anxiety, dyslexia, schizophrenia, Tourette's syndrome and smoking cessation. The "nicotinic" effect with respect to Alzheimer's is hypothesized. Parkinson's Disease is "presently of unknown etiology" and recent studies have exhibited dosing problems as well as "unusually high placebo effects". The pathophysiology of Tourette's syndrome is unknown. The treatment of ulcerative colitis is currently "limited to anti-inflammatories, immunosuppressants and antibiotics". Additionally, there are other pathological non-CNS conditions, such as pouchitis and influenza virus-induced pneumonitis, where nicotine efficacy has been reported, but remains to be confirmed.

Claims 1-4 and 6-15 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

2. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 12-15 the applicants' amendments and remarks have been fully considered but they are not found persuasive. The applicants' state that "in the absence of proof, supplied by the Examiner, of non-operability, this argument in support of non-enablement does not make unpatentable any of Claims 12 to 15 under 35 U.S.C. § 112, first paragraph" and also "many drugs have been patented for treatment of mental disorders which involve more than one portion of the brain". However, as discussed above the use of α -7 nicotinic acetylcholine receptor agonists are speculative. Symptomatic effects of drug abuse are a result of alterations in the functioning of the following neurotransmitters or their receptors: acetylcholine, dopamine, gamma-aminobutyric acid, norepinephrine, opioids and serotonin. Acetylcholinergic drugs antagonize acetylcholine receptors. Dissociative drugs affect all transmitter sites. Opiates act on both opioids and adrenergic receptor sites. Psychedelic drugs stimulate serotonin release, and sedative-hypnotic drugs potentiate the gamma-aminobutyric acid receptor. As stated by Giannini, specific signs and symptoms are associated with the neurotransmitters and receptors affected by each drug class.

Claims 12-15 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

3. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 12-15 the applicants' amendments and remarks have been fully considered but they are not found persuasive. The applicants' state that "the Official Action bars any patentable advance insofar as that patentable invention is new and previous attempts at treating these conditions have not been fully successful" and also that "such an analysis is inimical to the patent system". The applicants' seem to be expressing incredulity, concerning the need for enablement in any instant invention. The patent system allows for new inventions as long as the treatments are enabled. As stated above, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims where the disorder is treatable with a nicotinic acetylcholine receptor ligand. It is difficult to treat many of the disorders claimed herein. Recent studies on experimental and clinical pharmacology of nicotinic acetylcholine receptors cited in Annual Reports in Medicinal Chemistry indicate that the following disorders may be associated with nicotinic acetylcholine receptors: senile dementia of the Alzheimer's type, Parkinson's disease, Huntington's chorea, tardive dyskinesia, hyperkinesia, mania, depression, attention deficit disorder, anxiety, dyslexia, schizophrenia, Tourette's syndrome and smoking cessation. The "nicotinic" effect with respect to Alzheimer's is hypothesized. Parkinson's Disease is "presently of unknown etiology" and recent studies have exhibited dosing problems as well as "unusually high placebo effects". The

pathophysiology of Tourette's syndrome is unknown. The treatment of ulcerative colitis is currently "limited to anti-inflammatories, immunosuppressants and antibiotics".

Additionally, there are other pathological non-CNS conditions, such as pouchitis and influenza virus-induced pneumonitis, where nicotine efficacy has been reported, but remains to be confirmed.

Claims 12-15 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

4. The applicant's amendments and arguments are sufficient to overcome the 35 USC § 112, second paragraph rejection labeled a), b), c), e), f) and g) of the last office action, which are hereby **withdrawn**. However, with regards to the 35 U.S.C. § 112, second paragraph rejections labeled d), h), i), j), k), l), m), n), o), p), q), r), s), t), u), v), w), x), y), z), aa), ab) and ac), the applicants' amendments and remarks have been fully considered but they are not found persuasive.

d) The applicants' state that "the exact concentration of an effective amount of a schizophrenia treating compound of Claim 1 is not necessarily identical with a composition which employs the same compound to provide an α -7 nicotinic receptor agonizing amount of that compound". The composition claims 8, 10, 12 and 14 are to a compound of claim 1 and a pharmaceutically acceptable carrier. The statement of intended use of the resulting compositions is not given any patentable weight where that which is claimed is the compound plus its carrier.

h) to z) The applicants' state that "each of these compounds are recited in the specification, and include the objected to phrase of each of these subparagraphs, it is apparent that there is indeed sufficient antecedent basis to support these limitations of the compounds of Claim 17". However, each of these species are excluded by the proviso at the end of claim 1 and located in the specification.

aa) The applicants' state that "this rejection is couched in terms of the meaning of the limitation "dimethyl-biphenyl" in the species of the claim". However, each of these species are excluded by the proviso at the end of claim 1 and located in the specification.

ab The applicants' state that "ground of rejection is couched, in Subparagraph (ab), as providing an alleged insufficient antecedent basis for the limitation "bromo-phenyl" of the species of that claim". However, this species is excluded by the proviso at the end of claim 1 and located in the specification.

ac) The applicants' state that "the examiner must accept the recitation of the invention" and also that "it is incumbent upon the examiner to produce references or proof establishing the inoperability of the claimed compounds in the treatment of the diseases recited in these claims. The examiner must examine the application under 35 U.S.C. § 112, second paragraph, clear and concise manner pointing out the meets and bounds of the instant invention. Thus claims 9, 11, 13 and 15 are vague and indefinite in that the applicants have not set forth the meets and bounds of the instant invention.

Claims 8-15, 17 and 18 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, which applicant regards as the invention, for reasons of record and stated above.

5. The applicant's amendments and arguments are sufficient to overcome the 35 USC § 102, anticipation rejections labeled paragraphs 5) and 6) of the last office action, which are hereby **withdrawn**.

In view of the amendment dated April 26, 2004, the following new grounds of rejection apply:

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 17-20 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

Claims 17-20 are species, which are excluded by proviso spanning page 4, line 35 through page 5, line 6.

7. Claims 17-20 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claim 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reason(s) apply:

- a) Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the definition of Q where Q is a a straight.....
(Claims 1-5 and 7-15)
- b) Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the definition of the hetero atoms within the definition of R^3 and R^4 , which are not stated in the form of a Markush grouping, i.e. selected from the group consisting of NR^5 , O, S. (Claims 1-15)
- c) Claims 12-15 are vague and indefinite in that it is not known what is meant by the close parenthesis after "cocaine", which is unmatched with an open parenthesis.
- d) Claim 16 recites the limitation "nitro" in the fourth species. There is insufficient antecedent basis for this limitation in the claim.
- e) Claim 16 recites the limitation "methyl ester" in the ninth species. There is insufficient antecedent basis for this limitation in the claim.
- f) Claim 16 recites the limitation "isobutyl ester" in the tenth species. There is insufficient antecedent basis for this limitation in the claim.

g) Claim 16 recites the limitation "octyl ester" in the thirteenth species. There is insufficient antecedent basis for this limitation in the claim.

h) Claim 16 recites the limitation "ethyl ester" in the thirty sixth species. There is insufficient antecedent basis for this limitation in the claim.

i) Claim 16 recites the limitation "propyl ester" in the thirty seventh species. There is insufficient antecedent basis for this limitation in the claim.

In view of the lack of antecedent basis of the species of claims 16-20, the following rejections apply:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

9. Claim 20 is rejected under 35 U.S.C. 102(a) as being anticipated by Gallet et al., WO 00/58311. Gallet teaches the compound of the instant Q moiety is 4-bromo-phenyl. See example 2 on page 7 where R₃ is bromo.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:


(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gallet et al., WO 00/58311. The generic structure of Gallet encompasses the species of claims 17-20 and the fourth species of claim 16. Examples 1-23 differ only in the nature of the substituents R_1 , R_2 , R_3 , R_4 and R_5 . Page 1, lines 17-26 defines the substituents R_1 , R_2 , R_3 , R_4 and R_5 such that R_1 , R_2 , R_3 , R_4 and R_5 each represent a hydrogen or halogen atom or a group of trifluoromethyl, trifluoromethoxy, cyano, hydroxyl, alkyl, alkoxy, phenoxy, or phenyl which is optionally substituted by a halogen atom or a group of trifluoromethyl, cyano, hydroxyl, alkyl or alkoxy, or R_2 and R_3 form together a group of formula $-OCH_2O-$ or $-CH_2CH_2CH_2CH_2-$. The compounds of the instant invention are generically embraced by Gallet in view of the interchangeability of the R_1 , R_2 , R_3 , R_4 and R_5 substitutions of formula I. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example 2-methoxy, 3-bromo, etc. as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 571-272-0674. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Brenda Coleman
Primary Examiner Art Unit 1624
June 28, 2004